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Update on Development of a Tranquilizer Trap Device

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The foothold trap is an important tool that is used by the U.S. Department of Agriculture Animal Damage Control (ADC) program to capture coyotes (Canis latrans) that are causing livestock depredations. In FY 1990 and FY 1991 the ADC program trapped 17,732 and 15,805 coyotes, respectively (USDA 1991;1992). Foothold traps can cause trauma and injury to feet and legs (Englund 1982; Linhart et al. 1986; Olsen et al. 1986, 1988; Onderka et al. 1990, Tullar 1984) and Onderka et al. (1990) observed oral injuries such as broken teeth, and tongue and gum lacerations in captured animals. The ADC program and other organizations such as the U. S. Technical Advisory Group for Humane Trap Standards (Linhart 1990), are investigating means of reducing injuries to animals caught in traps. Two approaches to reduce injuries, trap modification and the use of a tranquilizer, have been investigated and previously tested in the field. Most of the studies have focused upon trap modifications. Several studies have evaluated the padded jaw trap (Linhart et al. 1986; 1988; Linhart and Dasch 1992; Olsen et al. 1986; Onderka et al. 1990; Tullar 1984). These studies show that padded foothold traps reduce, but do not eliminate injury to captured animals.

The use of a tranquilizer device attached to a foothold trap jaw was described by Balser in 1965. This research showed that the use of the tranquilizer, diazepam, reduced foot and leg injuries, struggling, aggression, escapes, and eased the release of nontarget species such as dogs (Canis familiaris). Diazepam is a U. S. Department of Justice, Drug Enforcement Administration (DEA) controlled substance (Seal and Kreeger 1987) and it never became authorized as a tranquilizer for traps. Savarie and Roberts (1979) evaluated several other tranquilizers under laboratory conditions as possible replacements for diazepam; their tests did not use foothold traps but instead used behavioral observations to determine Central Nervous System depression. Favorable results were obtained with propiopromazine hydrochloride (HCl), and it was later evaluated with foothold traps under field conditions by Linhart et al. (1981). Linhart's study tested propiopromazine HCl with four different types of delivery devices; with each type, 75 to 90% of animals had little or no foot damage at a 24-hr check period as compared to only 14% with little or no damage for controls in which the tranquilizer was not used. These investigators noted that additional studies were needed for development of a tranquilizer trap device. However, studies were discontinued and research efforts were directed toward evaluation of the padded jaw trap.

In recent years there has been renewed interest in the tranquilizer trap device by the ADC program. Zemlicka and Bruce (1991) conducted tests with pen-reared coyotes under laboratory conditions to evaluate delivery systems and formulations of tranquilizer trap devices containing propiopromazine HCl. Their results were encouraging but they recommended further field test evaluations before final recommendations could be made on the most effective tranquilizer trap devices.

This paper will give a general outline of the process that the Denver Wildlife Research Center (DWRC) proposes to initiate for the development of a tranquilizer for use in a trap device. The tranquilizer would be classified as a veterinary product regulated by the Food and Drug Administration (FDA) and must comply with the Federal Food, Drug and Cosmetic Act as described in 21 Code of Federal Regulations (CFR) 512. An Investigational New Animal Drug Application (INADA) is required to be filed as the initial step in gaining approval from the FDA to use an animal drug. This is the beginning of a lengthy process which includes dose titration studies and clinical trials to insure product efficacy and safety standards as established by FDA. FDA procedures are similar to those of the Environmental Protection Agency (EPA); however, the burden of proof for drug quality is on the drug manufacturer, not on the registrant and the FDA generally does not require environmental effects and fate data. Upon submission of a New Animal Drug Application (NADA) and approval, the drug would become legally available for use for designated wildlife species by authorized wildlife professionals. Described below are 8 phases of research effort that we anticipate will be required to develop a tranquilizer for the trap device.

Phase 1: Selection of a Suitable Drug

Although propiopromazine HCl has proved to be effective in field trials, this drug may no longer be available because of lack of a commercial demand. Also, there have been many tranquilizers developed in the past 10 to 15 years that may have better potential. Literature reviews will be conducted and contacts will be established with pharmaceutical companies in an attempt to find a suitable chemical. A suitable chemical includes the following factors: high potency, high margin of safety (ratio of lethal and effective dose), good stability, continued drug availability, patent status that will allow use without excessive cost, location of a company willing to supply the drug, availability of analytical methodology, and minimal hazards to nontarget species (i.e., dose that is lethal to nontargets should be higher than dose that would tranquilize target animal). Drugs that will be reviewed include: 1) First and second generation tranquilizers that have been available for over 30 years. Advantages would be that they are relatively inexpensive, and generally have no patent protection. However, many of these tranquilizers have a low level of biological activity, and may not be available from producers for more than 5 to 10 years; 2) Third and fourth generation tranquilizers have been available for 20 years or less. These tranquilizers are moderately expensive because many use or manufacturing patents are still in effect. They have a moderate level of biological activity, but would probably be available for 10 years or longer; and 3) Fifth and sixth generation tranquilizers are recently developed or experimental chemicals. These tranquilizers

are very expensive because of tight producer control, and long-term patent coverage. However, advantages would be a high level of biological activity (very low dosage rate), and they should be available for at least 10 to 20 years.

From the Phase I review, a decision-making matrix will be developed incorporating estimates for each candidate drug for cost per tranquilizer device, development and authorization costs, and use restrictions. At this point, a decision will be made regarding the candidate drugs of choice for efficacy and potential nontarget testing.

Phase 2: Testing of Candidate Drugs

To select the best possible candidate(s) for field evaluations, a limited number of drugs selected from the Phase I evaluation would be tested for efficacy on captive coyotes under laboratory conditions by procedures similar to those described by Savarie and Roberts (1979). Protocols for these dose titration tests would have to be approved by FDA.

Phase 3: Tranquilizer Delivery System and Analytical Methodology

Research will commence on a delivery device for the drug(s) of choice. As the delivery device is developed, an analytical assay method for the use formulation(s) will have to be developed.

Phase 4: Summary of Existing Information, Completion and Submission of INADA, and Request for Expedited Review

The INADA will be prepared (with all required supportive documentation) and submitted to FDA. A number of the FDA requirements will have to be addressed at this time, including location of a Source Manufacturer, and development of labeling and files to track the chemical. Telephone consultations and visits to FDA will be required. A request for Expedited Review, which limits the amount of time FDA may take to respond, may also be developed and submitted.

Phase 5: Design of Protocols, and Continued Research on Delivery System and Analytical Methodology

Protocols will have to be submitted to FDA for clinical trials of the tranquilizer trap device to support safety and efficacy claims. Negotiation and work sessions with FDA will occur during this phase. Research on a delivery system and validation of an analytical method for the formulation will continue. Nontarget hazards may need to be addressed, depending upon the projected use pattern.

Phase 6: Clinical Trials

Laboratory and field clinical trials will be conducted according to FDA approved protocols and with Quality Assurance monitoring. Data will be analyzed and summarized.

Phase 7: Completion and Submission of NADA and Expedited Review

A NADA will be submitted upon completion of summary of data supporting safety and efficacy claims. Among the requirements of 21 CFR 514, the following items will be addressed in the NADA: 1) Labeling, 2) Manufacturing Methods, Facilities and

Controls, 3) Analytical Methods for Residues, 4) Evidence to Establish Safety and Effectiveness, and 5) Environmental Impact Analysis (EIA).

Phase 8: Finalization of NADA and Submission of Documents for FDA Approval

Following negotiation with FDA regarding the NADA, any further data requirements will be met and a final revised report will be submitted to FDA. At this time, a Freedom of Information Statement and a final EIA will be submitted. In addition, it will probably be necessary during this phase to prepare an Environmental Assessment in compliance with the National Environmental Policy Act.

The total projected time and cost for development of a tranquilizer trap device is 4.5 years and $500,000 to $1,000,000. Timing for some of the phases can overlap, and will involve the interaction of several disciplines.

Summary

The ADC program is concerned about animal welfare and the humaneness of the methods it uses in its control and extension programs. A tranquilizer trap device has been proposed for attachment to foothold traps, snares and live traps to tranquilize animals to reduce the possibility of trap injuries. The device will be developed first for use on coyotes and subsequently for possible use on other species. A synopsis for development of a tranquilizer trap device is described that includes selection of a suitable drug, laboratory testing, development of appropriate applications for submission to the FDA, performance of field safety and efficacy trials, and approval of a NADA by the FDA.

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